Communications to the Editor

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REACTION OF METHYL VINYL KETONE CYANOHYDRIN PHOSPHATE WITH AROMATIC COMPOUNDS

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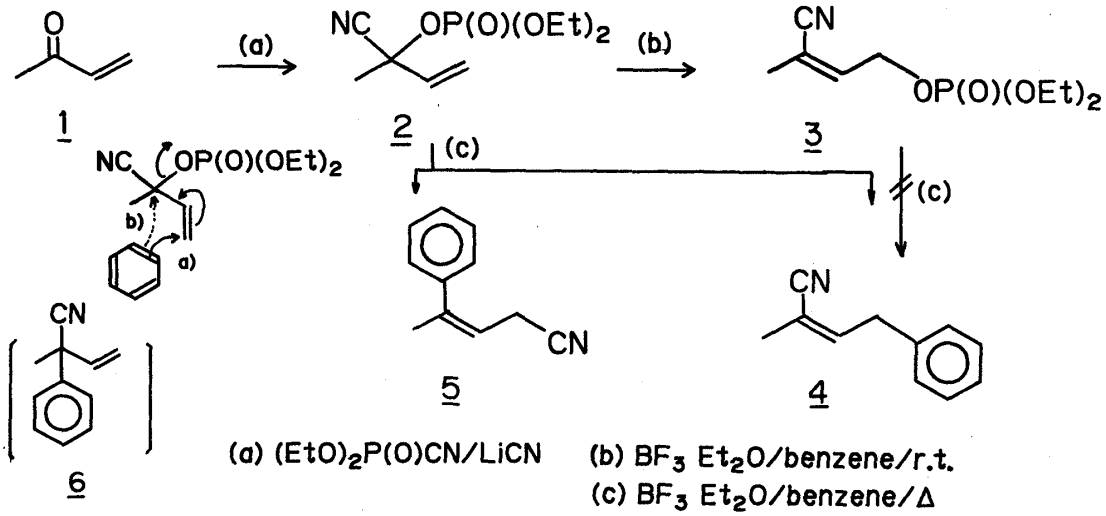
Methyl vinyl ketone cyanohydrin phosphate was found to react with aromatic compounds in the presence of borontrifluoride etherate to give 4-arylangelonitriles.

KEYWORDS —— methyl vinyl ketone; diethyl phosphorocyanidate; lithium cyanide; methyl vinyl ketone cyanohydrin phosphate; borontrifluoride etherate; allylic rearrangement; 4-arylangelonitrile

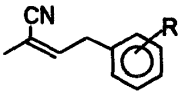
In a previous paper,[1] we reported that p-benzoquinone reacts with diethyl phosphorocyanidate [DEPC, $(EtO)_2P(O)CN$] in the presence of lithium cyanide (LiCN) to give p-benzoquinone cyanohydrin phosphate which reacts with aromatic compounds to give various kinds of biaryls. We recently found[2] that α,β-unsaturated ketones, such as 2-cyclopenten-1-one, 2-cyclohexen-1-one and cholest-4-en-3-one, react with DEPC/LiCN to give the corresponding cyanohydrin phosphates which, in benzene at room temperature, are readily transformed into conjugated allylic phosphate via a novel borontrifluoride (BF_3) etherate-catalyzed allylic rearrangement. The present paper describes the cyanophosphorylation of methyl vinyl ketone (1) and its application to the synthesis of 4-arylangelonitriles which are rarely found in the literature.

When 1 was treated with DEPC (1.5 eq) and LiCN (1.5 eq) in tetrahydrofuran at 0-5 °C, methyl vinyl ketone cyanohydrin phosphate (2)[3] was obtained in 84% yield after purification by silica gel column chromatography. When a solution of 2 was stirred with BF_3 etherate (3 eq) in benzene at room temperature, compound 3 was obtained in 58% yield as a sole product. The spectral data [IR ν_{max} cm^{-1} 2210 (CN), 1260 (P=O), 960-1020 (P-O-P). ^{1}H-NMR ($CDCl_3$) δ : 2.03 (3H, bs, $=CCH_3$), 4.75 (2H, m, CH_2), 6.33 (1H, m, =CH). High-resolution MS : m/z 233.0816 (Theor. 233.0818)] indicated the structure of 3 to be 4-diethylphosphonooxy-2-cyano-2-butene, which was obtained by the allylic rearrangement induced by BF_3 etherate.[2] This reaction also took place without a catalyst but at high temperature, and gave 3 in a low yield. On the other hand, when a benzene solution of 2 was boiled under reflux in the presence of BF_3 etherate (3 eq) for 5 h, 4-phenylangelonitrile (4)[4] [^{1}H-NMR ($CDCl_3$) δ : 1.97 (3H, bs, CH_3), 3.67 (2H, d, J=7.62 Hz, CH_2), 6.30 (1H, m, =CH), 7.19-7.34 (5H, m, Ar-H)] and 2-phenyl-2-butenenitrile (5) [^{1}H-NMR ($CDCl_3$) δ : 1.99 (3H, bs, CH_3), 3.51 (2H, d, J=7.25 Hz, CH_2), 6.53 (1H, m, =CH), 7.13-7.35 (5H, m, Ar-H)] were obtained in 59% and 5.5% yields, respectively.[5] Treatment of 3 with BF_3 etherate in a refluxing benzene afforded 3 in quantitative recovery. Therefore, it is apparent that phosphate (3) is not an intermediate in the formation of 4. The Z-stereochemistry of these olefins (3, 4, and 5), showing the large allylic coupling constants (J_{cisoid}=1.63-1.75 Hz)[6] between vinyl protons and methyl protons in their ^{1}H-NMR spectra as well as the small cis-$^3J_{CH_3,\ H}$ values of 5.8-5.9 Hz[7] in their



^{13}C-NMR spectra, was clearly indicated upon comparison with that of ethyl methacrylate [J_{cisoid}=1.63 Hz and $J_{transoid}$=1.00 Hz between vinyl proton and methyl protons in the ^{1}H-NMR spectrum, and cis-$^{3}J_{CH3,\ H}$=5.8 Hz and trans-$^{3}J_{CH3,\ H}$=10.1 Hz in the ^{13}C-NMR spectrum]. While the formation of 4 may be reasonably explained by the nucleophilic addition of benzene to the electrophilic position of 2 induced by the elimination of phosphate function (path a), analogous to the results of the biaryl synthesis previously described,[1] 5 would be obtained by the allylic rearrangement of cyanide anion of 6 which was initially formed via path b. The regio- and stereo-selective introduction of the benzene ring in this reaction is noteworthy. In accord with the case of benzene, the similar reactions of 2 with other aromatics are summarized in the Table. The structure of these 4-arylangelonitriles were readily determined on the basis of their ^{1}H-NMR spectra (300 MHz in $CDCl_3$).

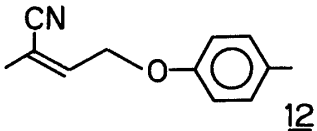
Table. 4-Arylangelonitriles from Methyl Vinyl Ketone Cyanohydrin Phosphate with Aromatic Compounds[a]



Entry	Substrate	Product (R=)	No.	Yield (%)
1	Benzene	H	4	51
2	Toluene[b]	4'-Methyl	7	75
3	p-Xylene[b]	2',5'-Dimethyl[d]	8	55
4	Naphthalene[c]	5',6'-C_4H_4[e]	9	38
5	Anisole[c]	2'-Methoxy	10a	61[f]
		4'-Methoxy	10b	
6	p-Methylanisole[c]	2'-Methoxy-5'-methyl	11a	33[f]
		3'-Methoxy-5'-methyl	11b	

a) All products are oily materials and gave satisfactory high-resolution MS spectra.
b) The reaction was carried out at 50°C in each substrate as solvent.
c) The reaction was carried out in acetonitrile at 50°C.
d) The product corresponding to 5 was isolated in 3.5% yield.
e) Notation C_4H_4 refers to the fused benzene ring.
f) This represents a combined yield of two isomers with the ratio of 8:2 in entry 5 and 1:1 in entry 6.

The reaction of 2 with the phenolic compounds was also investigated. Treatment of 2 with p-cresol under the same conditions as above gave p-tolyloxyangelonitrile (12) in 46% yield. On the other hand, the reaction of 2 with α-naphthol in the presence of BF_3 etherate in acetonitrile afforded a complex mixture from which only 2-hydroxy-1-(α-methyl-α-vinyl)naphthaleneacetic acid lactone (13)[8] was isolated, in 5.8% yield.



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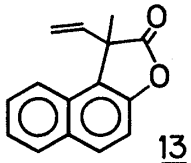

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In conclusion, we provided a convenient method for the preparation of 4-arylangelonitriles, some of which are otherwise difficult to obtain, using a methyl vinyl ketone cyanohydrin phosphate.

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REFERENCES AND NOTES

1) S. Harusawa, M. Miki, J. Hirai, and T. Kurihara, Chem. Pharm. Bull., 33, 899 (1985).

2) S. Harusawa, M. Miki, R. Yoneda, and T. Kurihara, Chem. Pharm. Bull., 33, 2164 (1985).

3) Compound 2 : IR ν_{max} cm^{-1} : 1280 (P=O), 1060-960 (P-O-P). ^{1}H-NMR ($CDCl_3$) δ : 1.36 (6H, t, J=7.5 Hz, 2 x $OCH_2\underline{CH_3}$), 1.89 (3H, bs, CH_3), 4.17 (4H, quint, J=7.5 Hz, 2 x $\underline{CH_2}CH_3$), 5.45 and 5.72 (each 1H, each d, J=10 and 17 Hz, $=CH_2$), 6.10 (1H, dd, J=10, 17 Hz, =CH). High-resolution MS : m/z 233.0816 (Theor. 233.0818).

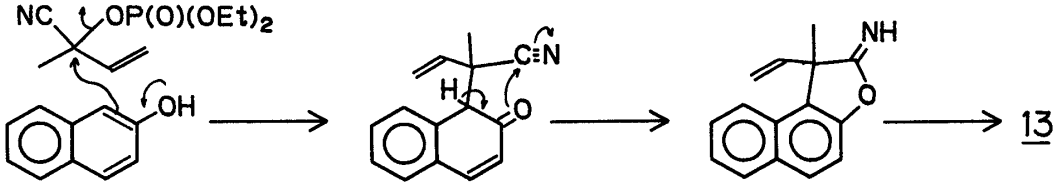
4) E. Vedejs and D.A. Engler, Tetrahedron Lett., 1977, 1241.

5) The definitive evidence that compound 5 is not an E-isomer of 4 was given by oxidation with Lemiex-von Rudloff reagent[9] yielding benzoic acid from the former and phenylacetic acid from the latter.

6) N.S. Bhacca and D.H. Williams, "Application of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., 1964, p.108.

7) J.L. Marshall, "Method in Stereochemical Analysis," Verlag Chemie International, Inc., Vol.2, 1983, p.37.

8) Compound 13 : IR ν_{max} cm^{-1} : 1800 (CO). ^{1}H-NMR ($CDCl_3$) δ : 5.17 and 5.36 (each 1H, each d, J=10 and 18 Hz, $=CH_2$), 6.16 (1H, dd, J=10, 18 Hz). High-resolution MS : m/z 224.0835 (Theor. 224.0837). The following scheme is considered to be a plausible mechanism of in the formation of 13.



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9) R.U. Lemiex and E.Von Rudloff, Can. J. Chem., 33, 1701, 1710 (1955).

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